APJAI
Asian Pacific Journal of
Allergy and Immunology

ORIGINAL ARTICLE

A multicenter study of crisaborole use in pediatric patients with atopic dermatitis in real-world setting in Thailand

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Abstract

Background: Increasing evidence supports the efficacy of crisaborole in atopic dermatitis (AD). Ethnic differences in AD endotypes may influence treatment outcomes, while data in Southeast Asian children remain limited.

Objective: To evaluate the efficacy and safety of crisaborole in Thai children aged >3 months with mild-to-moderate AD in a real-world multicenter setting.

Methods: This prospective observational study enrolled pediatric patients with mild-to-moderate AD were recruited from dermatology clinics at three tertiary hospitals in Bangkok between July 2023 and July 2024. Eligible patients applied crisaborole twice daily to all AD lesions. Outcomes included Investigator's Static Global Assessment (ISGA) success and improvements in pruritus and clinical signs at days 14 and 28. Disease severity was assessed using the Atopic Dermatitis Severity Index (ADSI) and Total Signs Score (TSS).

Results: Ninety Thai participants (median age 5.4 years; 54.4% girls) were enrolled. The intent-to-treat population included 89 and 84 participants at days 14 and 28, respectively. ISGA success rates were 10.1% and 38.1%, while pruritus severity improved in 50.6% and 71.4% of patients at days 14 and 28, respectively. Clinical signs improvement varied by feature and significant reductions in ADSI and TSS from baseline. Treatment-related adverse events occurred in 47.2% of patients, most commonly application-site redness (32.6%), burning/stinging (19.1%), and exudation (5.6%); all were mild and transient.

Conclusion: Crisaborole treatment was associated with improved clinical outcomes and was generally well tolerated. However, the observational design and lack of a control group preclude causal conclusions regarding efficacy. Controlled studies are needed to confirm these findings.

Key words: crisaborole, efficacy, safety, AD, Thai children

Citation:
Chatproedprai, S., Rujimethapass, N., Na Bangxang, P., Wananukul, S., Limpongsanurak, W., Wisuthsarewong, W., Singalavanija, S., Chantawarangul, K., Kanchanapoomi, K., Tempark, T., Sukneewat, C., Nitiyarom, R. (0000).
A multicenter study of crisaborole use in pediatric patients with atopic dermatitis in real-world setting in Thailand.
Asian Pac J Allergy Immunol, 00(0), 000-000.
https://doi.org/10.12932/ap-250326-2261

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Introduction

Atopic dermatitis (AD) is a common, highly pruritic, chronic relapsing inflammatory skin disease. AD usually presents in early childhood, 60% of cases present within the first year of life and 90% by 5 years of age.[1,2] In Thailand, the prevalence of eczema reported in children aged 6-7 years and 13-14 years was 16.7% and 9.6%, respectively.[3] The pathogenesis of this condition is complex and multifactorial, including epidermal barrier dysfunction, immune dysregulation, microbiome dysbiosis, and environmental triggers skin inflammation.[4] The diagnosis is based on pruritic symptoms, the characteristic of recurrent eczematous lesions with typical age-specific distribution, associated clinical signs, and a medical history. Hanifin and Rajka published a list of 23 clinical signs and symptoms of atopic dermatitis in 1980 and is still used in clinical practice. Atopic dermatitis can be classified into different endotypes according to ethnicity and age based on immunologic markers.[5] Therefore, the treatment of atopic dermatitis with various phenotypes should be more personalized rather than a 'one-size-fits-all' approach.[5]

Management of AD includes parental education about the natural course of the disease, the importance of improving skin barrier function through proper skin care and avoidance of potential aggravating factors. Anti-inflammatory therapy is an essential part of the treatment which topical corticosteroids are the mainstay of treatment. Topical calcineurin inhibitors are alternative treatment in case of steroid phobia, having steroid side effects, steroid unresponsive or parental preference. In severe cases or unresponsive to topical treatment, systemic agents may be considered. Today, it is widely accepted that the prevalence of steroid phobia is increasing in clinical practice. Therefore, nonsteroidal treatment should be the answer in the era of increasing steroid phobia.

Crisaborole is a nonsteroidal, anti-inflammatory agent which enhances cellular control of inflammation by inhibiting phosphodiesterase 4–dependent cyclic adenosine monophosphate (cAMP) degradation.[6] This leads to increased level of intracellular cAMP and thus suppresses downstream regulation of the nuclear factor-κB and nuclear factor of activated T cell signaling pathways through protein kinase A.[7] It was approved by US FDA in 2016 to use in children older than 2 years old with mild-to-moderate AD[6] and extended to children older than 3 months old in 2020.[8] There have been increasing evidence supporting the efficacy of crisaborole in the treatment of AD.[7,9-19] In Thailand, crisaborole was approved by Thai FDA in July 2023.

As mentioned above, there might be a difference in AD endotypes according to ethnicity and there has been no study determining its efficacy in Southeast Asia. We would like to present Thailand as a representative country from Southeast Asia, which is a tropical region with high humidity. In addition, crisaborole is in the ointment formulation and may have different treatment-related adverse effects from Western countries. The researchers would like to assess the efficacy and safety of crisaborole in Thai AD children older than 3 months old with mild-to-moderate severity in a real-world experience in a multicenter, cross-sectional, observational study.

Methods

Study design

A multicenter, prospective, observational study of AD children in 3 tertiary care hospitals (King Chulalongkorn Memorial Hospital, Siriraj Hospital, and Queen Sirikit National Institute of Child Health) in Bangkok, Thailand was conducted between 1 July 2023 and 31 July 2024 after the ethical approval from each hospital.

Participants

Atopic patients aged 3 months-18 years old with a baseline Investigator's Static Global Assessment (ISGA) score of mild and moderate severity (**Supplemental Table**) attended as OPD/IPD patients in 3 tertiary care hospitals and agreed to participate were enrolled. All of them had a clinical diagnosis of AD by either pediatric dermatologists or allergists according to Hanifin and Rajka criteria.[12] All patients had a wash out period of topical anti-inflammatory treatment ≥ 2 weeks, systemic treatment included biologic agents ≥ 4 weeks. Cases with active skin infection or immunocompromised patients were excluded from the study.

Sample size was calculated by using the formula for one group to have a proportion of success by 0.31[7] and an acceptable error by 0.1 at the 95% confidence level. A sample size of 90 subjects was required [3 centers, 30 patients each center].

The study protocol was approved by the Institutional Review Board from each center (Faculty of Medicine, Chulalongkorn University (COA No. 0909/2023); Faculty of Medicine, Mahidol University, Siriraj Hospital (COA No. Si 683/2023); and Queen Sirikit National Institute of Child Health (IRB No.058/2567)). All adhere to the provisions outlined in the Declaration of Helsinki. Written informed consent was given by all subjects or their legal guardians prior to enrollment.

Intervention

Patients who met the inclusion criteria and agreed to participate in the study were assessed demographic data, age at diagnosis, duration of AD, type and frequency of emollient use, baseline ISGA score, itching symptoms, history of sleep disturbance and photography. Emollients were categorized into three groups: 1) basic moisturizers, defined as widely available formulations primarily intended for general skin hydration and which may contain fragrances or colorants; 2) intensive moisturizers, characterized by higher viscosity and greater occlusivity than basic formulations and typically free of fragrances and colorants; and 3) moisturizer-plus formulations, consisting of advanced products containing functional ingredients, such as ceramides and/or anti-inflammatory agents, and typically free of fragrances and colorants. Patients were provided and instructed to apply a layer of crisaborole to cover each AD lesion twice daily throughout the study. Patients were allowed to continue the emollient use as in the previous application, except for the areas treated with crisaborole. Regarding antihistamine use, patients were permitted to continue their existing antihistamine therapy or use antihistamines as an adjunctive treatment. However, all antihistamine use was required to be documented in the study diary.

In the event of a skin infection, patients were permitted to receive topical and/or systemic antibiotics accordingly to the severity of the infection. In cases of severe infection, crisaborole treatment was temporarily discontinued in affected area. In the event of disease flare-ups, patients were allowed to visit the study physician before their scheduled appointment. The decision to continue or discontinue crisaborole treatment was made based on the physician's clinical assessment and/or the preference of the patient's guardian. However, the concomitant use of other anti-inflammatory agents was not permitted during the study period. Patients whose physicians or guardians decided to discontinue crisaborole treatment were considered early withdrawals and were withdrawn from the study. In the event of concomitant infections (e.g., respiratory tract or gastrointestinal tract infections), patients were permitted to use other medications as clinically indicated. All such medications were required to be recorded in the study diary.

Treatment adherence will be assessed through review of patient diaries. Reasons for nonadherence (e.g. the absence of active lesions, misunderstanding of treatment instructions or other contributing factors) will be identified and managed accordingly. Patients will be instructed by the study physicians to apply crisaborole to affected lesions twice daily throughout the study period. Treatment discontinuation was defined as permanent cessation of the study treatment before the end of the study period. Adherence was assessed only during the period in which participants remained on treatment. Participants who discontinued treatment contributed adherence data up to the date of discontinuation. Patients withdrawn because of disease flare-ups, at the discretion of the study physician or guardians, were excluded from the adherence analysis.

The efficacy of treatment was assessed by ISGA score, pruritus severity scale, and signs of AD, including treatment-related adverse events by diary record at day 14 ± 2 and day 28 ± 2. Participants who experienced intercurrent infections were retained in the analysis. In contrast, participants who developed disease flare-ups leading to treatment withdrawal, as determined by the study physician or at the request of the guardian, were excluded from the analysis.

Outcome measures

The primary end point will be defined as "success" if patients have ISGA score as clear (0) or almost clear (1) with a 2-grade or more improvement from baseline (S**upplemental Table**) and assess proportion of patients who achieved success at day 14 ± 2 and 28 ± 2. The secondary end points will assess improvement in pruritus severity scale (**Supplemental Table**) and signs of AD (**Supplemental Table**) which were measured on a 4-point scale of none (0), mild (1), moderate (2), and severe (3). Additionally, any adverse events occurring during the study period will be documented.

Improvement in these measures was defined as achieving none (0) or mild (1) with a 1-grade or more improvement from baseline. The change from baseline in the severity of each sign of AD was calculated as percentage change at day 14 ± 2 and 28 ± 2.

The Atopic Dermatitis Severity Index (ADSI) and Total Signs Score (TSS) were used as the end points to assess disease severity. The ADSI score is the sum of 5 component scores using a 4-point severity scale of erythema, excoriation, exudation, lichenification, and pruritus.[20,21] The TSS is the sum of 5 component scores using a 4-point severity scale of erythema, excoriation, exudation, lichenification, and induration/papulation.[22] The sum of these ratings generated a total score on a 16-point scale (0-15 points).

Statistical analysis

Categorical data will be presented as frequency or percentage, while continuous data will be presented as either median and interquartile range (IQR) or mean and standard deviation depending on data distribution.

The Chi square test will be used to compare the proportion of patients who achieved success, had improvement in pruritus severity scale and signs of AD at day 14 ± 2 and 28 ± 2. The percentage of change from baseline in the severity of each sign of AD, TSS and ADSI will be evaluated by Paired *t*-test at day 14 ± 2 and 28 ± 2.

All statistical analyses were done by using STATA version 18.0. A $p < 0.05$ was considered statistically significant.

Results

Participants and clinical characteristics

A total of 90 Thai pediatric participants were enrolled (median age, 5.4 years [IQR, 1.3–9.4]; 54.4% girls). The intent-to-treat participants consisted of 89 and 84 participants in the first (lost to follow-up 1) and second visit (adverse events 3, disease flare-up 2) respectively. Approximately 60 percent of participants had comorbidity which allergic rhinitis and food allergy being the 2 most common comorbidities (**Table 1**). Fifty-six (62.2%) and 34 (37.8%) participants were classified as mild and moderate severity of AD by ISGA score (**Supplemental Table**). Sixty percent of cases reported to have moderate and severe pruritus severity scale (**Supplemental Table**).

Efficacy endpoints

Investigator's Static Global Assessment (ISGA)

The percentage of patients achieving ISGA success was 10.1 (9/89; 95%CI 4.7-18.3) % at day 14 and 38.1 (32/84; 95%CI 27.7-49.3) % at day 28 (**Figure 1**). The proportion of patients with ISGA of clear (0) or almost clear (1) at day 28 was 66.7% (56/84).

Subgroup analysis of ISGA success according to disease severity (mild vs. moderate), as determined by ISGA grading, demonstrated a significantly higher proportion of ISGA success among patients with moderate disease severity than among those with mild disease severity at both day 14 ($p = 0.012$) and day 28 ($p = 0.009$) (**Table 2**). However, subgroup analyses according to age group (infants [≤ 1 year] vs. older children [> 1 year]), type of moisturizer (non–fragrance-free, fragrance-free, or therapeutic moisturizer), frequency of daily emollient application (≤ 1, 2, or > 2 times/day), presence of comorbidities, or lesion location (arm, leg, or other sites) showed no statistically significant differences.

Table 1. Participants' characteristics.

Characteristics	N = 90
Age (years), median (IQR)	5.4 (1.3-9.4)
Age at diagnosis (years)	
- Median (IQR)	1.29 (0.29-4.0)
Type of emollient, n (%)	
- No	2 (2.2)
- Basic moisturizer	37 (41.1)
- Intense moisturizer	13 (14.4)
- Moisturizer plus	38 (42.2)
Frequency of moisturizer use before participating in this Study, n (%)	
- No	2 (2.2)
- Less than or equal 1 time per day	15 (16.7)
- 2 times per day	52 (57.8)
- More than 2 times per day	21 (23.3)

Characteristics	N = 90
Comorbidity, n (%)	
- No	38 (42.2)
- Food allergy	25 (27.8)
- AR	27 (30.0)
- Asthma	2 (2.2)
- OSA	1 (1.1)
Use of antihistamine, n (%)	
- No	48 (53.3)
- Yes	42 (46.7)
Location of lesions, n (%)	
- 1 location	83 (92.2)
- 2 locations	7 (7.8)
Sites of lesions, n (%)	
- Arm	42 (46.7)
- Leg	41 (45.6)
- Face	7 (7.8)
- Head and neck	5 (5.6)
- Trunk and back	2 (2.2)

IQR, interquartile range; AR, allergic rhinitis; OSA, obstructive sleep apnea

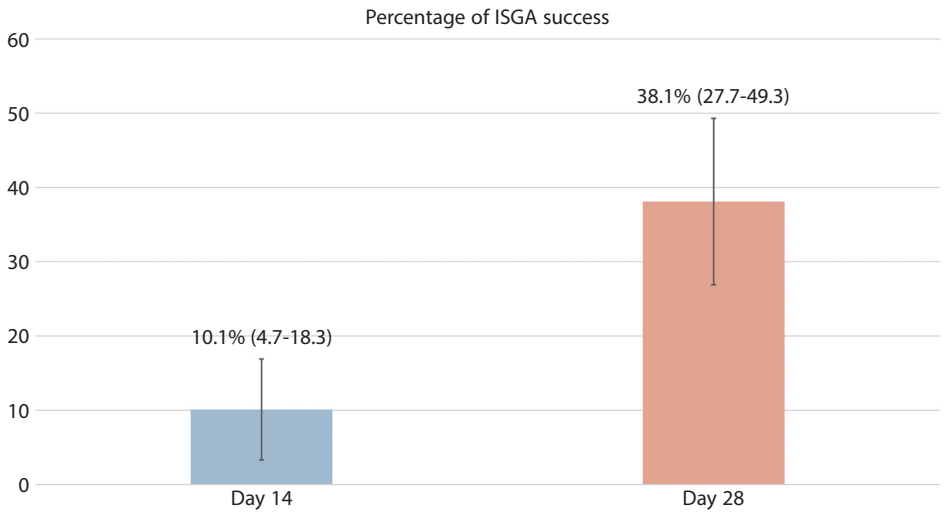

Figure 1. Investigator's Static Global Assessment (ISGA) success at day 14 and day 28.

Table 2. Investigator's Static Global Assessment (ISGA) success according to ISGA grading at day 14 and day 28.

ISGA grading	Day 14 (N = 89)			Day 28 (N = 84)		
	ISGA success, n (%)			ISGA success, n (%)		
	Yes	No	*p*-value	Yes	No	*p*-value
Mild	2 (3.6)	54 (96.4)	0.012	15 (27.8)	39 (72.2)	0.009
Moderate	7 (21.2)	26 (78.8)		17 (56.7)	13 (43.3)	

Severity of pruritus

From 60.0% (54/90) of participants at baseline, nearly 24.0% and 12.0% reported to have moderate and severe pruritus severity scale at day 14 and 28 respectively (**Supplemental Table**). The percentage of patients achieving improvement in pruritus severity scale at day 14 and 28 were 50.6 (45/89; 95%CI 39.7–61.3) % and 71.4 (60/84; 95%CI 60.5–80.5) % respectively.

Subgroup analysis in 30 participants from King Chulalongkorn Memorial Hospital, the median time to achieve improvement in pruritus was 5 (95%CI 3–12) days.

Signs of AD, Total Signs Score (TSS), and Atopic Dermatitis Severity Index (ADSI)

There were 2 signs achieving the highest percentage of patients with improvement in signs of AD at day 28 from baseline were excoriation and induration/papulation (54.8%; 46/84). The lowest proportion was exudation (13.1%; 11/84) (**Figure 2**). The percentage of change from baseline in the mean severity of each sign of AD at day 14 and day 28 was demonstrated in **Figure 3**.

Mean difference in TSS from baseline were -1.8 (95%CI -2.3–(-1.4)) and -2.4 (95%CI -2.9–(-2.0)) at day 14 and day 28 simultaneously. The percentage of change from baseline in mean TSS was significantly different at day 14 ($p < 0.001$) and day 28 ($p < 0.001$) (**Figure 4**).

Mean difference in ADSI score from baseline were -2.5 (95%CI 3.1–(-2.0)) at day 14 and -3.4 (95%CI -4.0–(-2.8)) at day 28. The percentage of change from baseline in mean ADSI was significantly different at day 14 ($p < 0.001$) and day 28 ($p < 0.001$) (**Figure 4**).

Adherence rates

Treatment adherence ranged from 50% to 100%, with a mean adherence rate of 92.9% (SD, 13.3%).

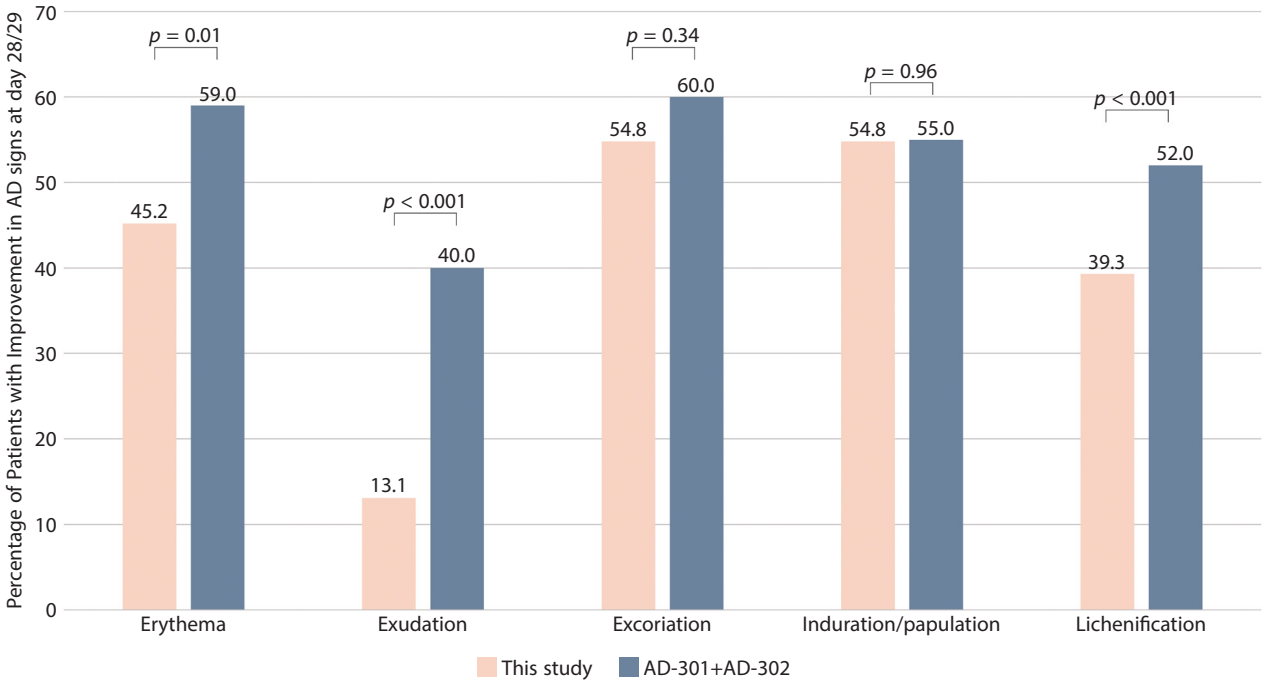

Figure 2. Percentage of patients with improvement in AD signs at day 28 comparing with Paller's study.[7]

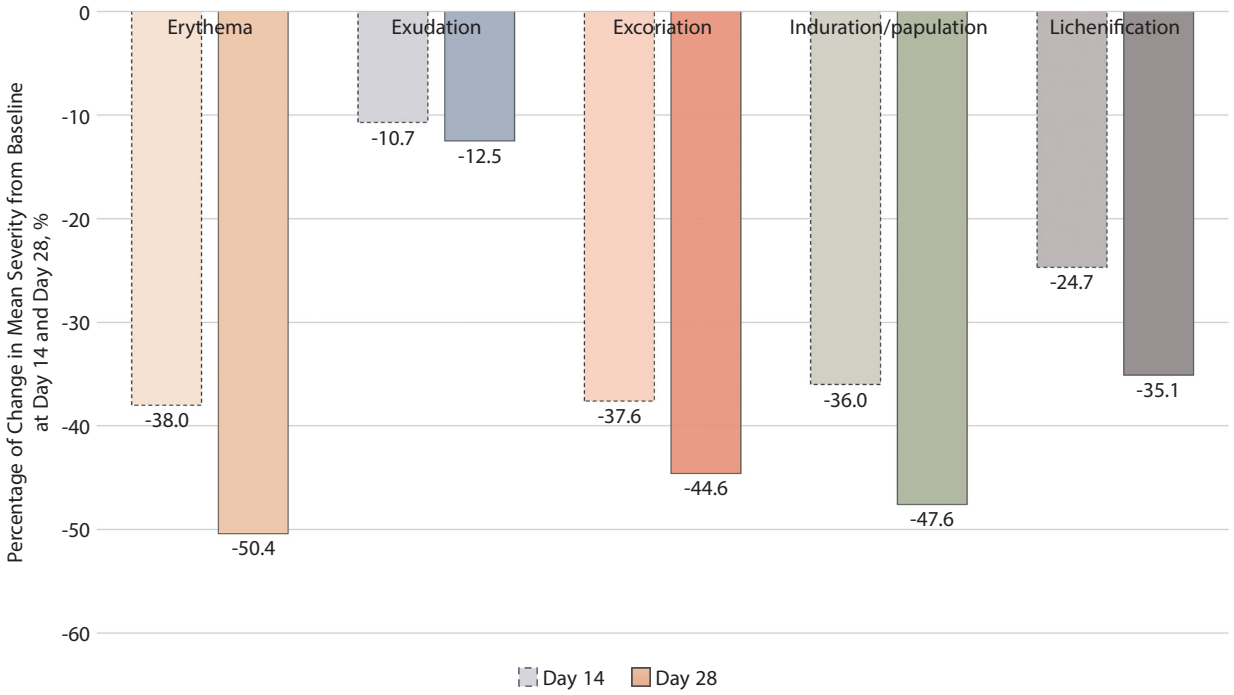

Figure 3. Percentage of change from baseline in the mean severity of each sign of AD at day 14 and day 28.

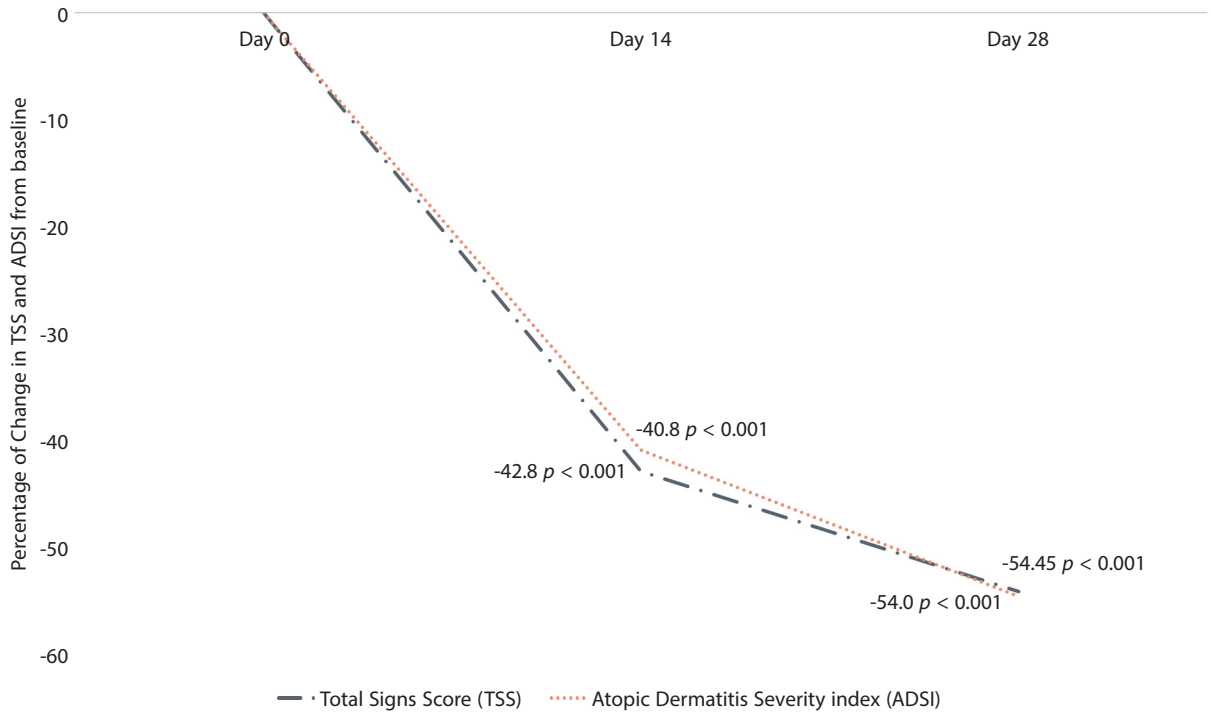

Figure 4. Percentage of change from baseline in mean Total Signs Score (TSS) and mean Atopic Dermatitis Severity Index (ADSI) at day 14 and Day 28.

Safety endpoints

Treatment-related adverse events were reported in 42 participants (47.2%). Application-site redness was the most frequent reported side effect (32.6%; 29/89), followed by application-site burning/stinging (19.1%; 17/89) and application-site exudation (5.6%; 5/89). However, these adverse events were mild and transient, 88.1% of participants (37/42) who reported these adverse events could complete the study. Of the 5 cases who did not complete the second visit, the treatment-related adverse events were application-site pruritus (60.0%; 3/5) and flare of lesions (40.0%; 2/5).

The prevalence of application-site adverse events did not differ significantly between younger children (< 2 years) and older children across most categories, including redness, burning/stinging sensation, itchiness, and pustules. However, exudation was significantly more common in younger children than in older children (13.0% vs. 1.7%, respectively; $p = 0.030$). There was no significant difference in the prevalence of adverse effects according to anatomical location (arms, legs, face, trunk).

Discussion

This multicenter study of crisaborole in pediatric AD patients in a real-world setting in Thailand demonstrated that crisaborole was effective and well tolerated for the treatment of mild-to-moderate pediatric AD older than 3 months old. The primary end point to assess the success of ISGA assessment was 10.1% and 38.1% at day 14 and day 28 consequently. This success was comparable with the previous studies in US,[7,21] China[18,23] and Japan.[23] Surprisingly, subgroup analysis of ISGA success according to disease severity as determined by ISGA grading, demonstrated a significantly higher proportion of ISGA success among patients with moderate disease severity than among those with mild disease severity at both day 14 and day 28. This finding may have been influenced by the definition of ISGA success, which required both an ISGA score of 0/1 and a ≥ 2-grade improvement from baseline. Given the requirement for a ≥ 2-grade improvement, patients with mild disease may have been less likely to achieve this endpoint than those with moderate disease.[24] In addition, because ISGA assessment is a physician-assessed visual scoring system and therefore inherently subjective, differences may have been more readily detected among patients with moderate disease severity than among those with mild disease severity.

Improvement in pruritus severity scale was 50.6% and 71.4% at day 14 and day 28 respectively. Improvement in signs of AD were different in each sign. Excoriation and induration/papulation achieved the highest percentage of patients with improvement (54.8% each). These findings were consistent with the study from North America[7] in the percentage of patients with improvement in excoriation and induration/papulation. A previous study, evaluating the efficacy of crisaborole for the treatment of mild-to-moderate AD across racial and ethnic groups, also demonstrated that crisaborole improved induration/papulation in nonwhite patients.[25] However, the percentage of patients with improvement in lichenification, erythema and exudation were significantly lower in this study. This might be explained by the different baseline characteristics of participants and different environmental factors which might become relevant factors. The hot climate and high humidity in Thailand may have influenced treatment tolerability, as the ointment formulation of crisaborole can produce a sticky sensation, potentially leading to increased rubbing during application among some participants including scratching behavior in children who were unable to tolerate the sensation. These factors may also partly explain the less pronounced improvement in exudation observed in this study. Consistent with this observation, a statistically significant increase in this application-site adverse event was noted among younger children (< 2 years) and will be discussed in a subsequent section.

The present study evaluated disease severity by ADSI and TSS which showed a significant decrease from baseline. These emphasized the efficacy of crisaborole in decreasing disease severity from baseline regardless of the evaluation score. Mean difference in TSS and ADSI score was consistent with the previous studies.[21,24]

Treatment adherence in this study was quite high, with a mean adherence rate of 92.9%. This suggests that most participants were able to incorporate crisaborole treatment into their daily routine and that the observed clinical outcomes were unlikely to have been substantially influenced by poor adherence.

According to the safety data from the North America studies (AD-301, AD-302),[7] which were phase-3, multicenter, randomized, double-blinded, vehicle-controlled trials evaluating the safety and efficacy of crisaborole 2% ointment compared to a vehicle ointment in patients older than 2 years with mild to moderate AD, the prevalence of treatment-related adverse events in this study was higher, although the severity of adverse events was comparable. These findings should be interpreted with caution. Although biological differences,[23,26] including potential variations in skin barrier characteristics among Asian populations, may contribute to differences in local tolerability profiles, the available evidence remains limited. Proposed mechanisms include a higher sweat gland density and a thinner stratum corneum in Asian skin, which may increase susceptibility to local irritation.[23,27]

Notably, the difference in adverse event rates remained apparent when compared with studies conducted in other Asian populations.[18,23] Several factors may account for this observation. As discussed previously, Thailand's tropical climate, characterized by high temperature and humidity, together with the ointment formulation of crisaborole, may influence treatment tolerability. In addition, regional differences in skin barrier characteristics may exist even among Asian populations living in different climatic environments. Alternative explanations should also be considered, including differences in adverse event reporting practices, the prospective observational design with scheduled follow-up assessments, variations in treatment adherence and application patterns, environmental factors, and differences in patient characteristics across study populations.

Therefore, the observed disparity in adverse event rates is likely multifactorial, and further studies are warranted to better understand the factors influencing crisaborole tolerability across different populations.

Application-site adverse events in patients with exudation were significantly more common among younger children (< 2 years) than older children. In addition to the possible explanations discussed earlier, younger children generally have thinner, more permeable skin and an immature skin barrier, which may increase their susceptibility to irritants and allergens.[28] No significant difference in the prevalence of application-site adverse events according to anatomical site distribution was observed in this study. This finding may be explained by the limited number of lesions involving sensitive areas such as the face and neck.

Crisaborole was evaluated as a maintenance therapy to reduce the incidence of flares in patients with AD who previously responded to crisaborole applied twice daily in the US. The median time of flare-free maintenance was 111 days. This study did not have a long duration to evaluate long-term efficacy as a maintenance therapy which might not have similar results regarding different ethnicity and/or different weather conditions.

This study included only Asians especially Southeast Asian populations; these results might not be generalized to all Asian populations as well as other tropical countries. In addition, this study was a real-world observational study without a comparator group and had a relatively short follow-up period, limiting the assessment of long-term efficacy and safety. Future studies incorporating an appropriate comparator group and longer follow-up duration are warranted to further evaluate the long-term effectiveness and safety of crisaborole in pediatric patients with atopic dermatitis.

Conclusion

In this real-world observational study, treatment with crisaborole was associated with favorable clinical outcomes and was generally well tolerated in children aged > 3 months with mild-to-moderate AD in Thailand. Crisaborole may represent a potential treatment option for mild-to-moderate pediatric AD, particularly for patients or caregivers concerned about topical corticosteroid use. Application-site redness and pain were the most common treatment-related adverse events; however, these events were generally mild and transient. Given the observational design and the absence of a control group, the findings should be interpreted with caution, and further controlled studies are needed to confirm the efficacy and safety of crisaborole in this population.

Conflict of interest

The authors declare that this study received funding and crisaborole ointment from Pfizer (Thailand) Limited (TH_86862499). However, the funder had no role in the study design, data collection, data analysis, interpretation of data or in writing the manuscript.

Author contributions

The authors confirmed contribution to the paper as follows: All authors have made substantial contributions to conception and design of the study including the enrolment of the subjects. S.C. performed the data collection, analyzed, and drafted the manuscript. All authors have approved the final version of this article.

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Supplemental Table

Table 1. Investigator's Static Global Assessment.

Scale	Grade	Definition
0	Clear	Minor residual hypopigmentation/hyperpigmentation; no erythema or induration/papulation; no oozing/crusting
1	Almost clear	Trace faint pink erythema, with barely perceptible induration/papulation and no oozing/crusting
2	Mild	Faint pink erythema with mild induration/papulation and no oozing/crusting
3	Moderate	Pink-red erythema with moderate induration/papulation with or without oozing/crusting
4	Severe	Deep or bright red erythema with severe induration/papulation and with oozing/crusting

To assess the patient's overall disease severity across all treatable atopic dermatitis lesions, Investigator's Static Global Assessment (ISGA) was assessed at screening and days 14 ± 2, and 28 ± 2. ISGA was assessed on a 5-point scale from clear (0) to severe (4).

Table 2. Severity of pruritus scale.

Scale	Grade	Definition
0	None	No itching
1	Mild	Occasional, slight itching/scratching
2	Moderate	Constant or intermittent itching/scratching that is not disturbing sleep
3	Severe	Bothersome itching/scratching that is disturbing sleep
4	Severe	Deep or bright red erythema with severe induration/papulation and with oozing/crusting

Severity of pruritus was recorded twice daily via diary by patients or caregivers before crisaborole was applied from days 1-28. Severity of pruritus was assessed on a 4-point scale from none (0) to severe (3).

Table 3. Signs of atopic dermatitis scale.

Scale	Grade	Definition
Erythema (redness)		
0	None	No redness
1	Mild	Mildly detectable erythema; pink
2	Moderate	Dull red; clearly distinguishable
3	Severe	Deep, dark red; marked and extensive

Table 3. (Continued)

Scale	Grade	Definition
Exudation (oozing and crusting)		
0	None	No oozing or crusting
1	Mild	Minor or faint signs of oozing
2	Moderate	Definite oozing or crusting
3	Severe	Marked and extensive oozing or crusting
Excoriation (evidence of scratching)		
0	None	No evidence of excoriation
1	Mild	Mild excoriation
2	Moderate	Definite excoriation
3	Severe	Marked, deep, or extensive excoriation
Induration/papulation		
0	None	None
1	Mild	Slightly perceptible elevation
2	Moderate	Clearly perceptible elevation but not extensive
3	Severe	Marked and extensive elevation
Lichenification (epidermal thickening)		
0	None	No epidermal thickening
1	Mild	Minor epidermal thickening
2	Moderate	Moderate epidermal thickening; accentuated skin lines
3	Severe	Severe epidermal thickening; deeply accentuated skin lines

Signs of atopic dermatitis were assessed at screening and days 14 ± 2, and 28 ± 2. Signs of atopic dermatitis were assessed on a 4-point scale from none (0) to severe (3).